α-SUBSTITUTED NAPHTHYLOXY ϖ-SUBSTITUTED ALKYL/ARYL AMINO-SUBSTITUTED ALKANE DERIVATIVES AS AGENT FOR TREATMENT OR PROPHYLAXIS OF DIABETES AND RELATED METABOLIC DISORDERS.

FIELD OF INVENTION

This invention relates to novel ϖ-substituted-naphthyloxy-amino alkanes, their preparation and use as antihyperglycemic agents and for the treatment and prevention of cardiovascular disorders (CVS) such as lipid lowering effects .

BACKGROUND OF THE INVENTION:

An analysis of the molecular structure of active PPARγ-agonists mentioned above would suggest the presence of three distinct substructures. (I) the thiazolidine 2, 4-dione unit 'A', (ii) the intermediate alkyl chain 'B' and (iii) the aryl substituent 'C'. Since the thiazolidine 2,4-dione derivatives are associated with side effects such as liver toxicity etc, a molecular modification to eliminate such a unit was considered desirable. In the present invention the thiazolidine 2, 4-dione unit has been replaced by substituted amino residues which has resulted in novel compounds showing the desired anti-hyperglycemic activity along with lipid lowering activity which is an added desirable activity.

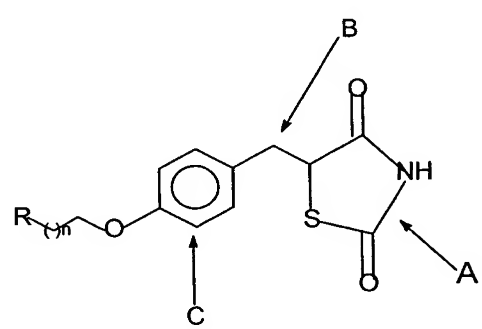


Fig-1 : Structure of PPARy-agonists

Prior Art

PPARγ-agonists which act as insulin sensitizers are showing promise in the treatment of NIDDM (Type II diabetes) which is a disease prevalent in developed as well as developing

countries. A number of agents show PPARγ agonist activity. Most of these compounds are thiazolidine 2, 4-dione derivatives. Some of the compounds belonging to this class which have entered in clinic are Pioglitazone (Momose, Y.; Takeda, H.; Hatanaka, C.; Oi, S.; Sohda, T. Chem.Pharm.Bull.1991, 39, 1440-1445), Rosiglitazone (Cantello, B.C.C.; Cawthorne, M.A.; Haigh, D.; Hindley, R.M.; Smith, S.A.; Thurlby, P.L. Bio-org. Med.Chem.Lett.1994,4,1181-1184), Netoglitazone (Viton, R.; Widdowson, P.S.; Ishii, S.; Tanaka, H.; Wikllain, G. British J. Pharmacolgy 1998, 125, 1708-14), Troglitazone(Yoshida, T.; Fujita, T.; Kanai, T.; et al J. Med. Chem. 1989, 32, 421-428).

OBJECT OF THE INVENTION

The object of the present invention relates to novel ϖ-substituted-naphthyloxy-amino alkanes derivatives having structural formula I.

Another object of the present invention relates to the process of preparing novel ϖ-substituted-naphthyloxy-amino alkanes derivatives having structural formula I.

Another object of the present invention relates to the process of preparing novel ϖ-substituted-naphthyloxy-amino alkanes derivatives having structural formula I.

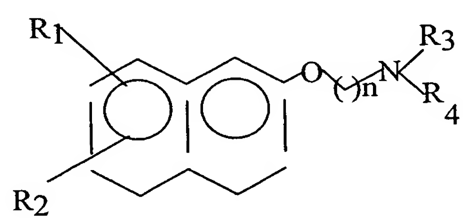
Yet another object of the present invention relates to the to a pharmaceutical composition for the treatment or prevention of cardiovascular disorders (CVS) and of hyperglycemic condition (diabetes) in mammals, including humans, said composition comprising of administering effective dosage of novel ω-naphthyloxy amino alkane derivatives having structural Formula 1 optionally along with acceptable salt/s, carrier/s or dilutent/s. .

Still another object of the present invention relates to a method for treatment or prevention of cardiovascular disorders and hyperglycemia (diabetes) by administering pharmaceutical effective dosage of ω-naphthyloxy amino alkane derivatives having structural Formula 1,

DESCRIPTION OF THE INVENTION:

This invention relates to novel ϖ-substituted-naphthyloxy-amino alkanes, their preparation and use as antihyperglycemic agents and for the treatment and prevention of cardiovascular disorders (CVS) such as lipid lowering effects. The main objective of the present invention is to provide agents to act in NIDDM with the added advantage of their effect in lowering low density cholesterol (LDL) without affecting high density cholesterol (HDL) in the treatment and prevention of CVS disorders.

Accordingly, the main embodiment of present invention relates to novel ω-naphthyloxy amino alkane derivatives having structural formula I,



I

Wherein R_1 and R_2 are individually H, a lower alkyl containing 1-6 carbon atoms, such as methyl, ethyl, propyl, butyl, pentyl, hexyl; a branched chain lower alkyl such as isopropyl, isobutyl, t-butyl and alkyl chains thereof.; a cyclic alkane such as cyclopropyl, cyclobutyl, cyclohexyl, cycloheptyl and cyclic alkanes thereof.; a lower alkoxy in which the alkyl group is as mentioned above, n is 1 to 6; R_3 and R_4

are individually H, a lower straight or branched chain alkyl containing 1-15 carbon atoms as mentioned above; a cyclic alkane as defined above; an aryl residue selected from group comprising of phenyl, substituted phenyl, naphthyl; an arylalkyl residue selected from group comprising of benzyl, substituted benzyl, form a part of a heterocylic ring selected from group comprising of pyrrolidine, piperidine, form a heterocylic ring with additional heteroatoms O,N,S selected from group comprising of piperazine,morpholine, oxazole, oxathinazole, oxathiazine etc.; an alkoxy carbonyl alkane selected from R_6COOR_7, wherein R_6 is $(CH_2)n$ (n=1-3) and R_7 is a lower alkyl as defined above.

Another embodiment of the present invention relates to preferred novel ω-naphthyloxy amino alkane derivatives comprising of

(i) N-(4-Methoxyphenyl)-[3-(naphthalen-2-yloxy)propyl]amine [I:R_1=R_2=R_3=H, R_4= 4-methoxyphenyl, n=3]

(ii) N-(4-Methoxyphenyl)-N-propyl[3-(naphthalen-2-yloxy) propyl amine.[I: R_1= R_2=H, R_3= propyl R_4= 4-methoxyphenyl, n=3]

(iii) N-(4-Methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amino} acetic acid ethyl ester. [I: R_1=R_2=H, R_3=CH_2COOEt,R_4=4-methoxy phenyl, n=3]

(iv) N-Benzyl-[2-(naphthalen-2-yloxy)-ethyl]amine[I:R_1=R_2=R_3=H, R_4= benzyl, n=2]

(v) N-(4-Methoxyphenyl)-[2-(naphthalen-2-yloxy) ethyl] amine [I: R_1 = R_2 = R_3 = H, R_4= 4-methoxy phenyl, n=2]

(vi) N-(4-Methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amine [I: R_1 = R_2 = R_3 =H, R_4=4-methoxy phenyl, n=3]

(vii) N-(4-Methoxyphenyl)-[4-(naphthalen-2-yloxy)butylamine [I:R_1=R_2=R_3=H, R_4= 4-methoxyphenyl, n=4]

(viii) N-(4-Methylphenyl)-[2-(naphthalen-2-yloxy)ethyl]amine[I:R_1=R_2=R_3=H, R_4=4-methyl phenyl, n=2]

(ix) N-(4-Methylphenyl)-[3-(naphthalen-2-yloxy) propyl] amine [I:R_1= R_2= R_3 = H, R_4=4-methyl phenyl, n=3]

(x) N-(4-Methylphenyl)-[4-(naphthalen-2-yloxy)butyl]amine[I:R_1=R_2=R_3=H, R_4=4-methyl phenyl, n=4]

(xi) N-(3-Methoxybenzyl)-[2-napthalen-2-yloxy)ethyl]amine[I:R_1=R_2=R_3=H, R_4=3-methoxy benzyl, n=2]

(xii) N-(3-Methoxybenzyl)-[3-napthalen-2-yloxy)propyl] amine[I:R_1=R_2= R_3= H, R_4=3-methoxy benzyl, n=3]

(xiii) N-(3-Methoxybenzyl)-[4-napthalen-2-yloxy)butyl]amine[I:R_1=R_2=R_3=H, R_4=3-methoxy benzyl, n=4]

(xiv) N-Benzyl-[2-(naphthalen-2-yloxy)-ethyl]amine [I:R_1=R_2=R_3=H,R_4= benzyl, n=2]

(xv) N-Benzyl-[3-(naphthalen-2-yloxy)-propyl] amine [I:R_1=R_2=R_3=H,R_4= benzyl, n=3]

(xvi) N-Benzyl-[4-(naphthalen-2-yloxy)-butyl]amine[I:R_1=R_2=R_3=H,R_4= benzyl, n=4]

(xvii) N-Cyclohexyl-[2-(naphthalen-2-yloxy)-ethyl]amine[I : R_1 = R_2 = R_3 = H, R_4 = cylohexyl ,n=2]

(xviii) N-Cyclohexyl-[3-(naphthalen-2-yloxy) propyl] amine [I : $R_1 = R_2 = R_3$ =H, R_4 = cylohexyl,n=3]

(xix) N-Cyclohexyl-[4-(naphthalen-2-yloxy)-butyl]amine[I:R_1=R_2=R_3=H, R_4 = cylohexyl,n=4]

(xx) N-(2-Ethyl-n-hexyl)-[2-(naphthalen-2-yloxy)ethyl]amine [I : $R_1 = R_2 = R_3$ = H,R_4=2-ethyl n-hexyl, n=2]

(xxi) N-(2-Ethyl-n-hexyl)-[3-(naphthalen-2-yloxy)propyl] amine[I:R_1=R_2= R_3= H, R_4=2-ethyl- n-hexyl, n=3].

(xxii) N-(2-Ethyl-n-hexyl)-[4-(naphthalen-2-yloxy)butyl] amine[I:R_1=R_2=R_3=H ,R_4=2-ethyl- n-hexyl, n=4]

(xxiii) N-(n-Dodecyl)-[2-(naphthalen-2-yloxy)-ethyl]amine [I:R_1=R_2=R_3= H,R_4= n-dodecyl,n=2]

(xxiv) N-(n-Dodecyl)-[3-(naphthalen-2-yloxy)-propyl] amine [I:R_1= R_2 = R_3 = H, R_4=n-dodecyl,n=3]

(xxv) N-(n-Dodecyl)-[4-(naphthalen-2-yloxy)-butyl]amine[I:R_1=R_2= R_3= H,R_4= n-dodecyl,n=4]

(xxvi) N-(Isoamyl)-[2-(naphthalen-2-yloxy)-ethyl]amine [I:R_1=R_2 = R_3 = H,R_4= isoamyl, n=2]

(xxvii) N-(Isoamyl)-[3-(naphthalen-2-yloxy)-propyl]amine[I:R_1=R_2=R_3=H R_4 = isoamyl, n =3]

(xxviii)N-(Isoamyl)-[4-(naphthalen-2-yloxy)-butyl]amine[I : $R_1 = R_2 = R_3$ = H , R_4 = isoamyl,n=4]

(xxix) N-(3-Phenylpropyl)-[2-(naphthalen-2-yloxy) ethyl] amine [I:R_1=R_2= R_3=H , R_4=2-phenyl ethyl, n=2]

(xxx) N-(3-Phenylpropyl)-[3-(naphthalen-2-yloxy) propyl] amine [I: R_1=R_2=R_3= H, R_4=2-phenylethyl, n=3]

(xxxi) N-(3-Phenylpropyl)-[4-(naphthalen-2-yloxy) butyl] amine [I: R_1=R_2=R_3=H, R_4=2-phenylethyl, n=4]

(xxxii) N-(n-Octyl)-[2-(naphthalen-2-yloxy) ethyl] amine [I: R_1=R_2=R_3=H, R_4=n-octyl, n=2]

(xxxiii)N-(n-Octyl)-[3-(naphthalen-2-yloxy) propyl]amine [I: R_1=R_2=R_3=H, R_4=n-octyl, n=3]

(xxxiv)N-(n-Octyl)-[3-(napthalen-2-yloxy) butyl] amine [I: R_1=R_2=R_3=H, R_4=n-octyl, n=4]

(xxxv) N-(n-Butyl)-[4-(naphthalen-2-yloxy) butyl] amine [I: R_1=R_2=R_3=H, R_4=n-butyl, n=4]

(xxxvi)N-(n-Propyl)-[4-(naphthalen-2-yloxy) butyl] amine [I: R_1=R_2=R_3=H, R_4=n-propyl, n=4]

(xxxvii) N-(2-Phenylethyl)-[2-(naphthalen-2-yloxy) butyl] amine [I, R_1=R_2=R_3=H, R_4=2-phenyl- ethyl, n=4]

(xxxviii) N-(Piperidinyl)-[4-(naphthalen-2-yloxy) butyl] amine [I, R_1=R_2=R_3=H, R_4= Piperidinyl, n=4]

(xxxix)N-(n-Butyl)-[3-(naphthalen-2-yloxy) propyl] amine [I, R_1=R_2= R_3= H, R_4 = n-butyl, n=3]

(xl) N-(n-Propyl)-[3-(naphthalen-2-yloxy) propyl] amine [I, R_1=R_2= R_3= H, R_4 = n-propyl, n=3]

(xli) N-(2-Phenylethyl)-[3-(naphthalen-2-yloxy) propyl] amine [I, R_1=R_2=R_3=H, R_4=2-phenyl ethyl, n=3]

(xlii) N-(Piperidinyl)-[3-(naphthalen-2-yloxy) propyl]amine [I, R_1=R_2=R_3=H, R_4= Piperidinyl, n=3]

(xliii) N-(4-Methoxyphenyl)-N-methyl[3-(naphthalen-2-yloxy)propylamine, [I, R_1 = R_2 = H, R_3= methyl, R_4=4-methoxyphenyl, n=3]

(xliv) N-(4 Methoxyphenyl)-N-ethyl[3-(naphthalen-2-yloxy) propyl amine. [I, R_1=R_2=H, R_3= ethyl, R_4=4-methoxyphenyl, n=3]

(xlv) N-(4-Methoxyphenyl)-N-propyl [3-(naphthalen-2-yloxy) propyl amine [I, R_1=R_2=H, R_3= propyl, R_4= 4-methoxyphenyl, n=3]

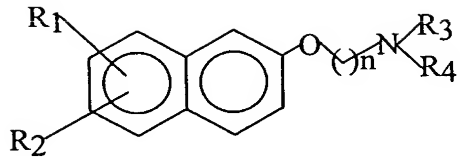
(xlvi) N-(4-Methoxyphenyl)-N-butyl[3-(naphthalen-2-yloxy) propyl amine[I,R_1=R_2=H, R_3= n-butyl, R_4=4-Methoxyphenyl, n=3]

(xlvii) N-(4-Methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amino} acetic acid ethyl ester[I, R_1=R_2=H, R_3= -CH_2COOEt, R_4=4-Methoxyphenyl, n=3]

(xlviii) 2,7-Bis[3-(4methoxyphenylamino)propyloxy]naphthalene[I,R_1=4-methoxyphenyl amino propyloxy, R_2 & R_3=H, R_4= 4-methoxyphenyl]

(xlix) 2,6-Bis[3-(4-methoxyphenylamino)propyloxy]naphthalene[I,R_2=4-methoxyphenyl amino propyloxy, R_1 & R_3=H, R_4= 4-methoxyphenyl]

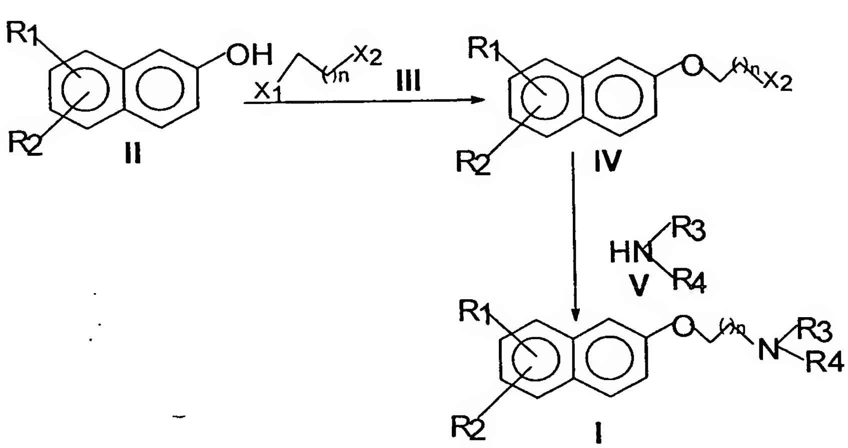
Another embodiment of the present invention relates to a method for preparing ω-naphthyloxy amino alkane derivatives having structural formula I,



I

Wherein R_1 and R_2 are individually H, a lower alkyl containing 1-6 carbon atoms, such as methyl, ethyl, propyl, butyl, pentyl, hexyl; a branched chain lower alkyl such as isopropyl, isobutyl, t-butyl etc.; a cyclic alkane such as cyclopropyl, cyclobutyl, cyclohexyl, cycloheptyl etc.; a lower alkoxy in which the alkyl group is as mentioned above, n is 1 to 6; R_3 and R_4 are individually H, a lower straight or branched chain alkyl containing 1-15 carbon atoms as mentioned above; a cyclic alkane as defined above; an aryl residue such as phenyl, substituted phenyl, naphthyl; an arylalkyl residue such as benzyl, substituted benzyl, form a part of a heterocylic ring such as pyrrolidine, piperidine, form a heterocylic ring with additional heteroatoms O,N,S such as piperazine,morpholine, oxazole, oxathinazole, oxathiazine etc.; an alkoxy carbonyl alkane such as R_6COOR_7, wherein R_6 is $(CH_2)n$ (n=1-3) and R_7 is a lower alkyl as defined above, said process comprising steps of:

(a) reacting substituted β-naphthol of Formula II with dihaloalkane of formula III in an organic solvent in the presence of a base to obtain an intermediate compound of formula IV, and



Wherein R_1 and R_2 are defined as above and wherein X_1 and X_2 may be same or different halogens, and

(b) reacting compound of formula IV with an amine of formula V in presence of an acid binding agent optionally in an organic solvent to obtain compound of formula I, wherein X_2 is a halogen and R_3 and R_4 are defined as above.

Another embodiment of the present invention relates to base in step (a) wherein the said base is selected from a group comprising of cesium carbonate, potassium carbonate, sodium carbonate, lithium carbonate or other bases.

Yet another embodiment of the present invention relates to the organic solvents in step (b) wherein the said organic solvents are selected from group comprising of dimethyl sulphoxide (DMSO), dimethylformamide (DMF), Hexamethylphosphoric triamide (HMPA) or acetonitrile.

Yet another embodiment of the present invention relates to temperature wherein the said temperature in step (a) is in range of about 50°C to 100°C,

Yet another embodiment of the present invention relates to temperature wherein the said temperature is preferably in the range of about 60°C to 80°C.

Still another embodiment of the present invention relates to temperature wherein the said temperature in step (b) in the range of about 120°C to 180°C.

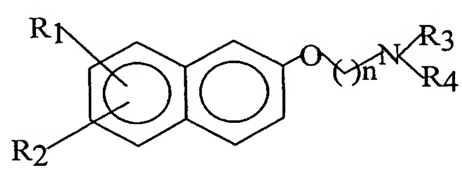
Still another embodiment of the present invention relates to temperature wherein the said temperature is preferably in the range of about 130°C to 150°C.

Still another embodiment of the present invention relates to the reaction time in steps (a) and (b) wherein said reaction time is in range of about 4 hours to 13 hours.

In one more embodiment of the present invention relates to the derivatives of formula (1) wherein the said derivatives have their melting points in the range of about 75°C to 270°C.

In one more embodiment of the present invention relates to the purity of the derivatives of formula (1) wherein the purity of the said derivatives is in the range of about 80% to 100%.

Another embodiment of the present invention relates to a pharmaceutical composition for the treatment or prevention of cardiovascular disorders (CVS) and of hyperglycemic condition (diabetes) in mammals, including humans, said composition comprising of administering effective dosage of novel ω-naphthyloxy amino alkane derivatives having structural Formula 1,

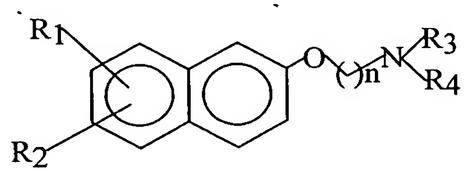


I

Wherein, R_1 and R_2 are individually H, a lower alkyl containing 1-6 carbon atoms, such as methyl, ethyl, propyl, butyl, pentyl, hexyl; a branched chain lower alkyl such as isopropyl, isobutyl, t-butyl etc.; a cyclic alkane such as cyclopropyl, cyclobutyl, cyclohexyl, cycloheptyl etc.; a lower alkoxy in which the alkyl group is as mentioned above, n is 1 to 6; R_3 and R_4 are individually H, a lower straight or branched chain alkyl containing 1-15 carbon atoms as mentioned above; a cyclic alkane as defined above; an aryl residue such as phenyl, substituted phenyl, naphthyl; an arylalkyl residue such as benzyl, substituted benzyl, form a part of a heterocylic ring such as pyrrolidine, piperidine, form a heterocylic ring with additional heteroatoms O,N,S such as piperazine,morpholine, oxazole, oxathinazole , oxathiazine and compounds thereof; an alkoxy carbonyl alkane such as R_6COOR_7, wherein R_6 is $(CH_2)n$ (n=1-3)

and R_7 is a lower alkyl as defined above, optionally along with acceptable salt/s, carrier/s or dilutent/s.

Yet another embodiment of the present invention relates to a method for treatment or prevention of cardiovascular disorders and hyperglycemia (diabetes) by administering pharmaceutical effective dosage of ω-naphthyloxy amino alkane derivatives having structural Formula 1,



I

Wherein R_1 and R_2 are individually H, a lower alkyl containing 1-6 carbon atoms, such as methyl, ethyl, propyl, butyl, pentyl, hexyl; a branched chain lower alkyl such as isopropyl, isobutyl, t-butyl etc.; a cyclic alkane such as cyclopropyl, cyclobutyl, cyclohexyl, cycloheptyl etc.; a lower alkoxy in which the alkyl group is as mentioned above, n is 1 to 6; R_3 and R_4 are individually H, a lower straight or branched chain alkyl containing 1-15 carbon atoms as mentioned above; a cyclic alkane as defined above; an aryl residue such as phenyl, substituted phenyl, naphthyl; an arylalkyl residue such as benzyl, substituted benzyl, form a part of a heterocylic ring such as pyrrolidine, piperidine, form a heterocylic ring with additional heteroatoms O,N,S such as piperazine,morpholine, oxazole, oxathinazole , oxathiazine and compounds thereof; an alkoxy carbonyl alkane such as R_6COOR_7, wherein R_6 is $(CH_2)n$ (n=1-3) and R_7 is a lower alkyl as defined above, optionally along with acceptable salt/s, carrier/s or dilutent/s.

Another embodiment of the present invention relates to the salts/carriers/diluents selected from a group consisting of lactose, sodium chloride, potassium chloride, magnesium sulphate, magnesium chloride, potassium sulfate, sodium sulfate, lithium sulphate, sodium phosphate, potassium phosphate, magnesium succinate, sodium carbonate, sodium sulfate, potassium acid phosphate or calcium bicarbonate.

Another embodiment of the present relates to derivatives wherein the said derivatives may be administered in form syrup, capsule, tablet, intravenous, liquid or suspension.

One more embodiment of the present invention relates to derivatives wherein method of administration for said derivatives may be oral, nasal, rectoral, or parenteral.

One more embodiment of the present invention relates to derivatives wherein said derivatives lower the concentration of cholesterol by about 30%.

One more embodiment of the present invention relates to derivatives wherein said derivatives lower the concentration of cholesterol preferably by about 26%.

Another embodiment of the present invention relates to derivatives wherein the said derivatives lower the concentration of phospholipid by about 35 %.

Another embodiment of the present invention relates to derivatives wherein the said derivatives lower the concentration of phospholipid preferably by about 30%.

Another embodiment of the present invention relates to derivatives wherein the said derivatives lower the concentration of Triglyceride by about 50 %

Yet another embodiment of the present invention relates to derivatives wherein the said derivatives lower the concentration of Triglyceride preferably by about 48%.

Yet another embodiment of the present invention relates to derivatives wherein the dosage of the said derivatives is in the range of about 250-350 μmol/Kg.,

Yet another embodiment of the present invention relates to derivatives wherein the dosage of the said derivatives is preferably about 300 μmol/Kg.

One more embodiment of the present invention relates to derivatives wherein said derivatives enhances the high-density lipoprotein (HDL) concentration by about 20 %.

Yet another embodiment of the present invention relates to derivatives wherein said derivatives enhances the high-density lipoprotein concentration preferably by about 14%.

Still another embodiment of the present invention relates to derivatives where said derivatives lowers the glucose (GLU) concentration to about 35 %.

Still another embodiment of the present invention relates to derivatives wherein said derivatives lowers the glucose concentration preferably to about 30%.

Another embodiment of the present invention relates to derivatives wherein said derivatives lowers the glycerol (GLY) concentration by about 18 %.

Yet another embodiment of the present invention relates to derivatives wherein the said derivatives lowers the glycerol concentration by about 14%.

Yet another embodiment of the present invention relates to derivatives wherein the said derivatives lower the glucose concentration in about 30 min to 10 hours during post drug administration.

Still another embodiment of the present invention relates to derivatives wherein the said derivatives lower the glucose concentration in about 1 hr to 7 hrs during post drug administration.

EXAMPLES

Example 1: 2-(2-Naphthyloxy)-1-chloroethane (IV: R_1=R_2=H, X_2= Cl, n=2).

A mixture of β-naphthol (1gm, 0.006 mole), anhydrous K_2CO_3 (10 gm, in excess) and 1-bromo-2-chloroethane (0.6 ml, 0.006 mole) was refluxed in dry acetone (50ml) for 6 hours. Reaction mixture was filtered and filtrate was concentrated to get oily compound, which was crystallized with benzene-hexane to give the colorless crystals of pure desired compound. m.p.94°C, (yield 1.36 gm, 96%).

Example 2: 3-(2-Naphthyloxy)-1-chloropropane (IV: R_1=R_2=H, X_2=Cl, n=3)

A mixture of β-naphthol (1gm, 0.006 mole), anhydrous K_2CO_3 (10 gm, in excess) and 1-bromo-3-chloropropane (0.7 ml, 0.006 mole) was refluxed in dry acetone (50ml) for 6 hours. Reaction mixture was filtered and filtrate was concentrated to get oily compound which was crystallized with benzene-hexane to give the colorless crystals of pure desired compound, m.p. 98°C, (yield 1.5 gm, 97%).

Example 3: 4-(2-Naphthyloxy)-1-chlorobutane (IV: R_1=R_2=H, X_2=Cl, n=4)

A mixture of β-naphthol (1gm, 0.006 mole), anhydrous K_2CO_3 (10 gm, in excess) and 1-bromo 4-chlorobutane (0.8 ml, 0.006 mole) was refluxed in dry acetone (50ml) for 6 hours. Reaction mixture was filtered and filtrate was concentrated to get oily compound, which was crystallized with benzene-hexane to give the colorless crystals of pure desired compound, m.p. 112°C, (yield 1.6 gm, 98%).

The method of preparation of compounds of formula I are given in these following examples.

Example 4: N-(4-Methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amine

[I: R_1=R_2=R_3=H, R_4=4-methoxy phenyl, n=3]

Method a:

A mixture of anhydrous potassium carbonate (10 gm, in excess) and p-anisidine (0.42 gm, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(4-methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl]amine as yellow solid, m.p.110 °C, (yield 0.66 gm, 95.6 %).

Example4:N-(4-Methoxyphenyl)-[3-(naphthalen-2-yloxy)propyl]amine

[I:R_1=R_2=R_3=H,R_4=4-methoxy phenyl, n=3]

Method b:

A mixture of anhydrous potassium carbonate (10 gm, in excess) and p-anisidine (0.42 gm, 0.003 mole) was taken in dry DMF (40 ml). Now 3-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(4-methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amine as yellow solid, m.p.110 °C, (yield 0.64 gm, 92.5 %).

Example5: N-(4-Methoxyphenyl)-N-propyl-3-(naphthalen-2-yloxy) propylamine.

[I:R_1=R_2,R_3=propyl R_4=4-methoxy phenyl, n=3]

A mixture of N-(4-methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amine (0.5 gm, 0.002 mole) and propyl bromide (0.54ml, 0.003 mole) was taken in dry acetone (40 ml). It was refluxed for 12 hrs and the progress of reaction checked by TLC. Reaction mixture was filtered and the filtrate was concentrated to get oily compound which was further crystallized by benzene hexane mixture to get N-(4-methoxyphenyl)-N-propyl [3-(naphthalen-2-yloxy) propyl amine, yellow solid, m.p.127 °C, (yield 0.67 gm, 95.7%).

Example 6: N-(4-Methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amino} acetic acid ethyl ester. [I: R_1=R_2=H, R_3= CH_2COOEt, R_4=4-methoxy phenyl, n=3]

A mixture of N-(4-methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amine (0.5 gm, 0.002 mole) and ethyl bromoacetate (0.62 ml, 0.003 mole) was taken in dry acetone (40 ml). It was refluxed for 10 hrs and the progress of reaction checked by TLC. Reaction mixture was filtered and the filtrate was concentrated to get N-(4-methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amino} acetic acid ethyl ester, yellow oil, (yield 0.75 ml, 96 %).

Example7: N-Benzyl-[2-(naphthalen-2-yloxy)-ethyl] amine [I: R_1=R_2=R_3=H, R_4= Benzyl, n=2]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and benzyl amine (0.38 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 2-(2-naphthyloxy)-1- chloroethane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-benzyl-[2-(naphthalen-2-yloxy)-ethyl] amine solid, m.p.94 °C, (yield 0.61 gm, 90.3 %).

Example8: N-(4-Methoxyphenyl)-[2-(naphthalen-2-yloxy)ethyl]amine [I:R_1=R_2=R_3=H, R_4= 4-methoxy phenyl, n=2]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and p-anisidine (0.45 gm, 0.003 mole) was taken in dry dimethylsulphoxide (DMSO, 40 ml). Now 2-(2-naphthyloxy)-1-chloroethane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 145°C for 7 hrs. The reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(4-methoxyphenyl)-[2-(naphthalen-2-yloxy) ethyl] amine yellow solid, m.p.92 °C, (yield 0.67 gm, 94 %).

Example 9: N-(4-Methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amine [I: R_1=R_2=R_3=H, R_4=4-methoxyphenyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and p-anisidine (0.42 gm, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloro propane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 135 °C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(4-methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amine yellow solid, m.p.110 °C, (yield 0.66 gm, 95.6 %).

Example10:N-(4-Methoxyphenyl)-[4-(naphthalen-2-yloxy)butylamine

[I:R_1=R_2=R_3=H, R_4=4-methoxyphenyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and p-anisidine (0.4 gm, 0.003 mole) was taken in dry DMSO (40 ml). Now 4-(2-naphthyloxy)-1-chlorobutane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 130 °C for 7 hrs. and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get as oily compound which was later crystallized by benzene hexane to get N-(4-methoxyphenyl)-[4-(naphthalen-2-yloxy)butyl]amine, yellow solid, m.p 95 °C, (yield 0.67 gm, 97.8 %).

Example11:N-(4-Methylphenyl)-[2-(naphthalen-2-yloxy)ethyl]amine

[I:R_1=R_2=R_3=H,R_4=4-methyl phenyl, n=2]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and p-toluedine (0.39 gm, 0.003 mole) was taken in dry DMSO (40 ml). Now 2-(2-naphthyloxy)-1-chloroethane (0.5 gm, 0.002 mole) was added in. Reaction mixture was refluxed at 140°C for 8 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(4-methylphenyl)-[2-(naphthalen-2-yloxy) ethyl]amine, yellow solid, m.p 92 °C, (yield 0.62 gm, 91.7 %).

Example12: N-(4-Methylphenyl)-[3-(naphthalen-2-yloxy)propyl]amine

[I:R_1=R_2=R_3=H, R_4=4-methyl phenyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and p-toluedine (0.36 gm,0.003 mole) was taken in dry DMSO(40 ml) .Now 3-(2-naphthyloxy)1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140 °C for 7 hrs.

and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get (4-methylphenyl)-[3-(naphthylen-2-yloxy) propyl] amine, m.p.100 °C, (yield 0.63 gm, 94.3 %).

Example13:N-(4-Methylphenyl)-[4-(naphthalen-2-yloxy)butyl]amine [I:R_1=R_2=R_3=H, R_4=4-methyl phenyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and p-toluedine (0.35 gm, 0.003 mole) was taken in dry DMSO(40 ml). Now 4-(2-naphthyloxy)-1-chlorobutane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 150 °C for 8 hrs. and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(4-methylphenyl)-[4-(naphthalen-2-yloxy) butyl] amine, m.p. 98°C, (yield 0.63 gm, 97 %).

Example14: N-(3-Methoxybenzyl)-[2-napthalen-2-yloxy)ethyl]amine[I:R_1=R_2=R_3=H, R_4=3-methoxy benzyl, n=2]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and m-methoxy benzyl amine (0.53 gm, 0.003 mole) was taken in dry DMSO (40 ml). Now 2-(2-naphthyloxy)-1-chloroethane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by

benzene hexane to get N-(3-methoxybenzyl)-[2-napthalen-2-yloxy) ethyl]amine, yellow solid, m.p.93 °C, (yield 0.58 gm, 88.6 %).

Example15:N-(3-Methoxybenzyl)-[3-napthalen-2-yloxy)propyl]amine [I:R_1=R_2=R_3=H, R_4=3-methoxy benzyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and m-methoxy-benzyl amine (0.45 gm, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 150°C for 8 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(3-methoxybenzyl)-[3-napthalen-2-yloxy)propyl]amine yellow, solid, m.p.97 °C, (yield 0.66 gm, 90.6 %).

Example27:N-(3-Methoxybenzyl)-[4-napthalen-2-yloxy)butyl]amine [I:R_1=R_2=R_3=H, R_4=3-methoxy benzyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and m-methoxy benzyl amine (0.46 gm, 0.003 mole) was taken in dry DMSO (40 ml). Now 4-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 150°C for 9 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(3-methoxybenzyl)-[4-napthalen-2-yloxy)butyl]amine ,yellow solid, m.p. 120 °C, (yield 0.68 gm, 94.5 %).

Example 17: N-Benzyl-[2-(naphthalen-2-yloxy)-ethyl] amine [I: R_1=R_2=R_3=H,R_4= benzyl, n=2]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and benzyl amine (0.38 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 2-(2-naphthyloxy)-1-chloroethane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-benzyl-[2-(naphthalen-2-yloxy)-ethyl] amine, solid, m.p.94 °C (yield 0.61 gm, 90.3 %).

Example 18: N-Benzyl-[3-(naphthalen-2-yloxy)-propyl] amine [I: R_1=R_2=R_3=H, R_4= benzyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and benzyl amine (0.36 ml, 0.003 mole) was taken in dry DMSO (40 ml).Now 3-(2-naphthyloxy)-1-chloro propane (0.5 gm, 0.002 mole) was added in it . Reaction mixture was refluxed at 140°C for 6 hrs. and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-benzyl-[3-(naphthalen-2-yloxy)-propyl]amine, solid, m.p. 109 °C, (yield 0.62 gm, 93.6 %).

Example 19: N-Benzyl-[4-(naphthalen-2-yloxy)-butyl] amine [I: R_1=R_2=R_3=H, R_4= benzyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and benzyl amine (0.34 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 4-(2-naphthyloxy)-1-chlorobutane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 150°C for 5 hrs. and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-benzyl-[4-(naphthalen-2-yloxy)-butyl]amine, solid, m.p.105 °C, (yield 0.62 gm, 95.3 %).

Example 20: N-Cyclohexyl-[2-(naphthalen-2-yloxy)-ethyl]amine [I:R_1=R_2=R_3=H, R_4=cylohexyl, n=2]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and cyclohexyl amine (0.32 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 2-(2-naphthyloxy)-1-chloro ethane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-cyclohexyl-[2-(naphthalen-2-yloxy)-ethyl] amine, solid, m.p. 89°C, (yield 0.56 gm, 85.6 %).

Example21: N-Cyclohexyl-[3-(naphthalen-2-yloxy)-propyl] amine [I: R_1=R_2=R_3=H, R_4=cylohexyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and cyclohexyl amine (0.29 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at

140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-cyclohexyl-[3-(naphthalen-2-yloxy)-propyl]amine, solid.m.p.98 °C (yield 0.61 gm,88 %).

Example22: N-Cyclohexyl-(4-(naphthalen-2-yloxy)-butyl)amine [I:R_1=R_2=R_3=H, R_4=cylohexyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and cyclohexyl amine (0.28 ml, 0.003 mole) was taken in dry DMSO (40 ml).Now 4-(2-naphthyloxy)1-chlorobutane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 150°C for 5 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-cyclohexyl-[3-(naphthalen-2-yloxy)-butyl]amine, solid. m.p., 94 °C, (yield 0.61 gm, 92 %).

Example23:N-(2-Ethyl-n-hexyl)-(2-(naphthalen-2-yloxy)ethyl)amine

[I:R_1=R_2=R_3=H,R_4=2-ethyl n-hexyl, n=2]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and 2-ethyl n-hexyl amine (0.37 ml,0.003 mole) was taken in dry DMSO(40 ml).Now 2-(2-naphthyloxy)-1-chloroethane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by

benzene hexane to get N-(2-ethyl- n-hexyl)-(2-(naphthalen-2-yloxy) ethyl] amine, solid, m.p.92 °C, (yield 0.62 gm, 83.6 %).

Example24:N-(2-Ethyl-n-hexyl)-(3-(naphthalen-2-yloxy)propyl)amine [I:R_1=R_2=R_3=H, R_4=2-ethyl- n-hexyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and 2-ethyl-n-hexyl amine (0.35 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(2-ethyl-n-hexyl)-(3-(naphthalen-2-yloxy) propyl) amine solid, m.p. 97 °C, (yield 0.6 gm, 84.8 %).

Example25:N-(2-Ethyl-n-hexyl)-(4-(naphthalen-2-yloxy)butyl])amine [I:R_1=R_2=R_3=H, R_4=2-ethyl-n-hexyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and 2-ethyl-n-hexylamine (0.33 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 4-(2-naphthyloxy)-1-chlorobutane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(2-ethyl-n-hexyl)-(4-(naphthalen-2-yloxy) butyl) amine, solid, m.p.94 °C, (yield 0.61 gm, 87.3 %).

Example26:N-(n-Dodecyl)-(2-(naphthalen-2-yloxy)-ethyl)amine [I:$R_1=R_2=R_3=H,R_4=$n-dodecyl, n=2]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and n-dodecyl amine (0.55 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 2-(2-naphthyloxy)-1-chloroethane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 8 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(n-dodecyl)–(2-(naphthalen-2-yloxy)-ethyl) amine, solid. m.p. 120 °C, (yield 0.78 gm, 89.3 %)

Example27:N-(n-Dodecyl)-(3-(naphthalen-2-yloxy)-propyl)amine

[I:$R_1=R_2=R_3=H,R_4=$n-dodecyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and n-dodecylamine (0.51 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(n-dodecyl)–(3-(naphthalen-2-yloxy)-propyl) amine, solid. m.p.126 °C, (yield 0.78 gm, 92.8 %).

Example28:N-(n-Dodecyl)-[4-(naphthalen-2-yloxy)-butyl]amine [I:$R_1=R_2=R_3=H,R_4=$n-dodecyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and n-dodecyl amine (0.48 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 4-(2-naphthyloxy)-1-chlorobutane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 150°C for 8 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(n-dodecyl)-(4-(naphthalen-2-yloxy)-butyl) amine, solid. m.p. 129 °C, (yield 0.78 gm, 95.5 %).

Example29:N-(Isoamyl)-(2-(naphthalen-2-yloxy)ethyl)amine

[I:R_1=R_2=R_3=H,R_4=isoamyl, n=2]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and isoamyl amine (0.24 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 2-(2-naphthyloxy)-1-chloroethane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 6 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(isoamyl)-(2-(naphthalen-2-yloxy)-ethyl) amine, solid, m.p. 91 °C, (yield 0.51 gm, 81 %).

Example30:N-(Isoamyl)-(3-(naphthalen-2-yloxy)-propyl)amine[I:R_1=R_2=R_3=H R_4=isoamyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and isoamyl amine (0.23 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloroethane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 150°C for 5 hrs and

the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get isoamyl-[3-(naphthalen-2-yloxy)-propyl] amine, solid, m.p. 95°C, (yield 0.53 gm, 85.6 %).

Example31:N-(Isoamyl)-(4-(naphthalen-2-yloxy)-butyl)amine

:R_1=R_2=R3=H,R_4=isoamyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and isoamylamine (0.21 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 4-(2-naphthyloxy)-1-chlorobutane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(isoamyl)-(4-(naphthalen-2-yloxy)-butyl) amine, solid, m.p. 102°C, (yield 0.54 gm, 89.3 %).

Example32:N-(3-Phenylpropyl)-(2-(naphthalen-2-yloxy)ethyl)amine[I:R_1=R_2=R_3=H, R_4=2-phenylethyl, n=2]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and 3-phenylpropylamine (0.47 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 2-(2-naphthyloxy)-1-chloroethane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 150°C for 6 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by

benzene hexane to get N-(3-phenylpropyl)-(2-(naphthalen-2-yloxy) ethyl) amine, solid, m.p. 104 °C, (yield 0.65 gm, 87.6 %).

Example33:N-(3-Phenylpropyl)-(3-(naphthalen-2-yloxy)propyl)amine [I:R_1=R_2=R_3=H, R_4=2-phenylethyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and 3-phenylpropyl amine (0.44 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 150°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(3-phenylpropyl)-(3-(naphthalen-2-yloxy) propyl) amine, solid, m.p. 109 °C, (yield 0.645 gm, 89.3 %).

Example34: N-(3-Phenylpropyl)-(4-(naphthalen-2-yloxy)butyl)amine[I:R_1=R_2=R_3=H, R_4=2-phenyl ethyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and 3-phenylpropyl amine (0.42 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 4-(2-naphthyloxy)-1-chlorobutane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 145°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(3-phenylpropyl)-(4-(naphthalen-2-yloxy) butyl) amine solid, m.p. 117 °C, (yield 0.67 gm, 93.6 %).

Example35: N-(n-Octyl)-(2-(napthalen-2-yloxy)ethyl) amine[I:R_1=R_2=R_3=H,R_4=n-octyl, n=2]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and n-octyl amine (0.37 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 2-(2-naphthyloxy)-1-chloroethane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(n-octyl)-2-(napthalen-2-yloxy)ethyl amine, solid, m.p.105°C, (yield 0.64 gm, 87.6 %).

Example36: N-(n-Octyl)-(3-(napthalen-2-yloxy) propyl) amine [I: R_1=R_2=R_3=H, R_4=n-octyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and n-octyl amine (0.35 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 6 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(n-octyl)-(3-(napthalen-2-yloxy) propyl) amine, solid, m.p.109 °C, (yield 0.63 gm, 89 %).

Example37: N-(n-Octyl)-(3-(napthalen-2-yloxy) butyl) amine [I: R_1=R_2=R_3=H, R_4=n-octyl, n=4

A mixture of anhydrous potassium carbonate (10 gm, in excess) and n-octyl amine (0.33 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 4-(2-naphthyloxy)-1-chlorobutane

(0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(n-octyl)-(3-(napthalen-2-yloxy)butyl) amine, solid, m.p 114 °C, (yield 0.65 gm, 93.4 %).

Example38:N-(n-Butyl)-(4-(naphthalen-2-yloxy)butyl)amine[I:R_1=R_2=R_3=H,R_4=n-butyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and n-butyl amine (0.32 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 4-(2-naphthyloxy)-1-chlorobutane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 8 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to oily compound which was later crystallized by benzene hexane to get N-(n-butyl)-(4-(naphthalen-2-yloxy) butyl) amine, solid. m.p. oil, (yield 0.56 gm, 96.5%).

Excample39:N-(n-Propyl)-(4-(naphthalen-2-yloxy)butyl)amine[I:R_1=R_2=R_3=H,R_4=n-propyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and n-propyl amine (0.26 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 4-(2-naphthyloxy)-1-chlorobutane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture

was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to oily compound which was later crystallized by benzene hexane to get N-(n-propyl)-(4-(naphthalen-2-yloxy)butyl)amine, solid, m.p. 118 °C, (yield 0.51 gm, 93.2 %).

Example40:N-(2-Phenylethyl)-(2-(naphthalen-2-yloxy)butyl)amine[I,R_1=R_2=R_3=H, R_4=2-phenylethyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and phenyl ethyl amine (0.4 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 4-(2-naphthyloxy)-1-chlorobutane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 140°C for 8 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to oily compound which was later crystallized by benzene hexane to get N-(2-phenylethyl)-(2-(naphthalen-2-yloxy) butyl) amine, solid, m.p. 139 °C, (yield 0.656 gm, 95.6 %).

Example41: N-(Piperidinyl-(4-(naphthalen-2-yloxy)butyl) amine [I:R_1=R_2=R_3=H, R_4= piperidinyl, n=4]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and piperidine (0.32 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 4-(2-naphthyloxy)-1-chlorobutane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 150°C for 7 hrs. and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to oily compound which was latter crystallized by benzene

hexane to get N-(piperidinyl)-(4-(naphthalen-2-yloxy) butyl) amine, oil, (yield 0.54 gm, 88.6%).

Example42: N-(n-Butyl)-(3-(naphthalen-2-yloxy) propyl) amine [I, R_1=R_2= R_3= H, R_4 = n-butyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and n-butylamine (0.34 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 135°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(n-butyl)-(3-(naphthalen-2-yloxy) propyl) amine, solid, m.p. 112 °C, (yield 0.55 gm, 94.5 %).

Example51: N-(n-Propyl)-(3-(naphthalen-2-yloxy) propyl) amine [I, R_1=R_2= R_3= H, R_4 = n-propyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and n-propyl amine (0.28 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 145°C for 8 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(n-propyl-(3-(naphthalen-2-yloxy) propyl) amine, solid, m.p.112°C, (yield 0.51 gm, 91.2 %).

Example44:N-(2-Phenylethyl)-(3-(naphthalen-2-yloxy)propyl)amine[I,R_1=R_2=R_3=H, R_4=2-phenyl ethyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and 2-phenylethyl amine (0.51 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 145°C for 7 hrs and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(2-phenylethyl)-(3-(naphthalen-2-yloxy) propyl) amine, solid, m.p.270 °C, (yield 0.65 gm, 93.7 %).

Example45:N-(Piperidinyl)-(3-(naphthalen-2-yloxy)propyl)amine[I,R_1=R_2=R_3=H, R_4= Piperidinyl, n=3]

A mixture of anhydrous potassium carbonate (10 gm, in excess) and piperidine (0.34 ml, 0.003 mole) was taken in dry DMSO (40 ml). Now 3-(2-naphthyloxy)-1-chloropropane (0.5 gm, 0.002 mole) was added in it. Reaction mixture was refluxed at 150°C for 8 hrs. and the reaction was completed as checked by TLC. Reaction mixture was poured in distilled water (60 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was later crystallized by benzene hexane to get N-(piperidinyl)-(3-(naphthylan-2-yloxy)propyl)amine, solid, m.p.78°C, (yield 0.53 gm, 85.7 %).

Example 46: N-(4-Methoxyphenyl)-N-methyl[3-(naphthalen-2-yloxy) propyl amine. [I,R_1=R_2=H, R_3= methyl, R_4=4-methoxyphenyl, n=3]

A mixture of (4-methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amine (0.5 gm, 0.002 mole) and methyl iodide (0.49 ml, 0.003 mole) was taken in dry acetone (40 ml). It was refluxed for 12 hrs and the progress of reaction checked by TLC. Reaction mixture was filtered and the filtrate was concentrated to get oily compound which was further crystallized by benzene hexane mixture to get N-(4 methoxyphenyl)-N-methyl (3-(naphthalen-2-yloxy) propyl) amine, crystallized as yellow solid, m.p. 112°C, (yield 0.69 gm, 94 %)

Example 47:N-(4 Methoxyphenyl)-N-ethyl(3-(naphthalen-2-yloxy) propyl) amine. [I, R_1=R_2=H, R_3= ethyl, R_4=4-methoxyphenyl, n=3]

A mixture of N-(4-methoxyphenyl)-[3-(naphthalen-2-yloxy)propyl]amine (0.5 gm,0.002 mole) and ethyl bromide(0.52 ml,0.003 mole) was taken in dry acetone(40 ml). It was refluxed for 12 hrs and the progress of reaction checked by TLC. Reaction mixture was filtered and the filtrate was concentrated to get oily compound which was further crystallized by benzene hexane mixture to get N-(4 methoxyphenyl)-N-ethyl [3-(naphthalen-2-yloxy) propyl amine, crystallized as yellow oil, (yield 0.64 gm, 94.6%).

Example49: N-(4-Methoxyphenyl)-N-propyl [3-(naphthalen-2-yloxy) propyl amine [I, R_1=R_2=H, R_3= propyl, R_4=4-methoxyphenyl, n=3]

A mixture of N-(4-methoxyphenyl)-[3-(naphthalen-2-yloxy) propyl] amine (0.5 gm, 0.002 mole) and propyl bromide (0.54 ml, 0.003 mole) was taken in dry acetone (40 ml). It was refluxed for 12 hrs and the progress of reaction checked by TLC. Reaction mixture was filtered and the filtrate was concentrated to get oily compound which was further crystallized by benzene hexane mixture to get N-(4-methoxyphenyl)-N-propyl[3-

(naphthalen-2-yloxy) propyl amine, crystallized yellow solid, m.p. 127 °C, (yield 0.67 gm, 95.7%)

Example50: N-(4- Methoxyphenyl)-N-butyl-(3-(naphthalen-2-yloxy) propyl) amine [I, R_1=R_2=H, R_3= n-butyl, R_4=4-Methoxyphenyl, n=3]

A mixture of N-(4-methoxyphenyl)-(3-(naphthalen-2-yloxy)propyl)amine (0.5 gm,0.002 mole) and butyl iodide(1 ml,0.003 mole) was taken in dry acetone(40 ml). It was refluxed for 12 hrs and the progress of reaction checked by TLC. Reaction mixture was filtered and the filtrate was concentrated to get oily compound which was further crystallized by benzene hexane mixture to get N-(4- methoxyphenyl)-N-butyl-(3-(naphthalen-2-yloxy) propyl) amine crystallized yellow solid, m.p. 127 °C, (yield 0.78 gm, 98 %).

Example51:{N-(4-Methoxyphenyl)-(3-(naphthalen-2-yloxy) propyl) amino} acetic acid ethyl ester[I,R_1=R_2=H, R_3= -CH_2COOEt, R_4=4-Methoxyphenyl, n=3]

A mixture of (4-methoxyphenyl)-(3-(naphthalen-2-yloxy) propyl) amine (0.5 gm, 0.002 mole) and ethyl bromoacetate (0.62 ml, 0.003 mole) was taken in dry acetone (40 ml). It was refluxed for 10 hrs and the progress of reaction checked by TLC. Reaction mixture was filtered and the filtrate was concentrated to get the oily compound {N-(4-methoxy phenyl)-(3-(naphthalen-2-yloxy) propyl) amino} acetic acid ethyl ester, oil (yield 0.75 ml, 96 %).

Example52:2,7,-Bis[3-(4-methoxyphenylamino)propyloxy]naphthalene[I,R_1=4-methoxyphenyl amino propyloxy, R_2 & R_3=H, R_4= 4-methoxyphenyl]

A mixture of 2,7-bis (3-chloropropyloxy)naphthalene (1 gm, 0.003 mole) and p-

anisidine (1.17gm, 0.005 mole) were taken in 60 ml dry DMSO. It was refluxed at 140 °C for 12 hrs the completion of the reaction was checked by TLC. The reaction mixture was poured into distilled water (80 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was further crystallized by benzene hexane to get the desired compound as solid, m.p. 127 °C, (yield 1.34 gm, 89 %).

Example53: 2,6-Bis[3-(4-methoxyphenylamino)propyloxy]naphthalene[I,R_2=4-methoxyphenyl amino propyloxy, R_1 & R_3=H, R_4= 4-methoxyphenyl]

A mixture of 2,6-bis(3-chloropropyloxy)naphthalene(1gm, 0.003 mole) and p- anisidine(1.17gm, 0.005 mole) was taken in 60 ml dry DMSO . It was refluxed at 140 °C for 12 hrs. The completion of the reaction was checked by TLC. The reaction mixture was poured into distilled water (80 ml) and extracted with ethyl acetate thrice. The organic layer was separated and concentrated to get oily compound which was further crystallized by benzene hexane to get the desired compound, m.p. 129 °C, (yield 1.4 gm, 91 %).

Biological Activity

A ANTIDIABETIC ACTIVITY

ANIMALS:

Adult male and female albino rats (Sprague Dawley) of body weight 160±20g, bred in CDRI animal house were used during the course of experiment; 6 animals were kept in one cage. All the animals were fed ad-lib standard pellet diet (Lipton, Bombay) and allowed unrestricted access to water. The following norms were followed for animal room environment. Temperature: 22 ± 1°C; Humidity: 50-50%; Light 300 Lux at floor level with regular 12 hours light cycle; noise level 50 decibels; ventilation 10-50 air changes per hour.

The blood–glucose lowering effects of the test samples/standard drugs were examined in the following two experimental models.

Sucrose–loaded rat model:

Overnight fasted male Sprague Dawley rats were used for the sucrose–loaded experiment. Blood was collected at '0'min from the tail vein of the animals. After the '0' min blood collection, samples/drugs were given to the test group consisting of 5 rats by oral gavage at a dose of 100 mg/kg. Half an hour post test sample treatment, a sucrose-load of 10.0 gm/kg body weight was given to each rat. The blood was collected at 30, 60, 90 & 120 min post sucrose-load.

Streptozotocin-induced diabetic rat model:

Single–dose effect; Sprague Dawley strain male albino rats of average body weight 160±20 g were selected for this study. A calculated amount of the fresh solution of STZ dissolved in 100 mM citrate buffer (ph 4.5) was injected to overnight fasted rats (60 mg/Kg) intraperitoneally. Blood was checked for glucose content 48 h later by glucometer & animals showing blood glucose profile above 250 mg/dl were selected and were divided into different groups. Blood-glucose levels were again tested at 1, 2, 3, 4, 5, 6, 7 and 24 h

post test sample/drug administration. Food but not water was withdrawn from the cages during the experiment.

Sucrose challenged Streptozotocin-induced diabetic rat model:

Single–dose effect; Sprague Dawley strain male albino rats of average body weight 160±20 g were selected for this study. A calculated amount of the fresh solution of STZ dissolved in 100 mM citrate buffer (ph 4.5) was injected to overnight fasted rats (60 mg/Kg) intraperitoneally. Blood was checked for glucose content 48 h later by glucometer & animals showing blood glucose profile between 150-250 mg/dl were selected and were divided into different groups. Half an hour post test sample treatment, a sucrose-load of 2.5 g/kg body weight was given to each rat. Blood-glucose levels were again tested at 30, 60, 90, 120, 180, 240, 300 min and 24 h post test sample/drug administration. Food but not water was withdrawn from the cages during the experiment.

(1) Hypoglycaemic activity of Test Compounds (compound no. 1 and 4), Glybenclamide and Gliclazide in normal rats:

The antidiabetic effect of test compounds (compound no.1 and 4) and standard drug Glybenclamide, Gliclazide on OGTT of normal rats was determined. At 100-mg/kg doses level, test compounds 1, 4, Glybenclamide and Gliclazide showed significant lowering 33.6%, 37.6%, 33.9% and 44.8% respectively, at 120 min post glucose load.

2) Hypoglycaemic activity of example 1, Glybenclamide and Gliclazide in STZ-induced diabetic rats:

The effect of Test compound 1 and standard antidiabetic drug Glybenclamide and gliclazide on blood glucose lowering in STZ-induced diabetic rats were determined. At 100 mg/kg dose level compound 1, Glybenclamide and gliclazide showed significant lowering on blood glucose. The lowering started from 1-hour that persisted up to 7-hours post drug administration. The lowering was of the order 28.0%, 32.8% and 27.7% respectively in case of test compound 1, Glybenclamide and gliclazide.

B. LIPID LOWERING ACTIVITY

Lipid lowering activity of compound-1 was evaluated in two different models *in vivo.*

(a)Triton Model: Male Charles foster rats weighing 200-225 g were divided into control, hyperlipedemic and hyperlipedemic plus drug treated groups containing six animals each. Hyperlipedemia was induced by administration of triton WR-1339(400mg/kg,IP). All animals were maintained on standard pellet diet and water ad lib.Test compound no.1 and Gugulipid (standard drug) were macerated with 2% aqueous gum acacia and this suspension was fed orally at the dose of 100mg/kg simultaneously with triton. The animals of control group received same amount of gum acacia. At the end of experiment, after 18 hrs , blood was withdrawn from retro orbital plexus and plasma was used for the assay of total cholesterol, phospholipid and triglyceride by standard spectrophotometric method.

Results: Administration of triton in rats produced marked hyperlipedemia as observed by the increased levels of plasma cholesterol, phospholipid and triglyceride by 2.92,3.32, 3.64 folds respectively (Table-1).

Treatment with compound -1 and gugulipid significantly lowered the plasma levels of cholesterol, phospholipid and triglyceride by 26,33 and 28% as well as 35,31,and 35% respectively in triton plus drug treated groups.

Table-1: Lipid lowering activity of test compound 1 (% lowering of plasma lipids)

Entry No.	Cholesterol	Phospholipid	Triglyceride
Test Compound1	26*	33**	28*
Gugulipid (standard drug)	35 **	31**	35**

* p<0.01, **<0.001 as compared to hyperlipemic group

(b) Dyslipemic Hamster Model: Male golden syrian hamster weighing 120-130 gm were divided into control, dyslipemic and dyslipemic plus drug treated group of 8 animals in each.

Dyslipemia was produced by feeding with fructose rich high fat diet(HFD).Dyslipemic hamsters had free acccess to HFD and water ad. Lib for 10 days(day1to day10). Compound 1 was macerated in vehicle containing 0.2%CMC + 0.4% tween-80 in distilled water and fed orally at the dose of 300□ mole/kg from day 4 to day 10 simultaneously with HFD feeding to hamster. Control animals received same amount of vehicle. At the end of the experiment on 10th day, blood was withdrawn and plasma was used for assay of triglyceride(Tg), cholesterol(chol), high density lipoprotein (HDL), glucose, glycerol and free fatty acids(FFA) by standard spectrophotometric methods on auto analyser. In another set of experiment antidyslipemic activity of fenofibrate at the dose of 1000□mole/kg was evaluated.

Results: Feeding with HFD produced marked dyslipemia in hamsters. Plasma level of Tg, chol, glycerol and FFA were shown to increase by 800,214, 167 and 215% respectively followed by a significant increase in the levels of glucose and HDL by 116 and 19% respectively. Feeding with test compound reduced levels of plasma Tg, chol, glycerol, HDL and glucose by 48,8,14,15 and 31% respectively. No significant change in FFA levels was observed. Similarly in another experiment with finofibrate (standard drug), the lowering in plasma, Tg, chol, glucose, glycerol and FFA was 77,30,33,52 and 53% respectively followed by 33% increase in plasma HDL in HFD fed dyslipemic hamsters.

Table-2: Activity profile of Test compound 1(per cent change in lipid biochemical parameters)

Compound	Dose (μmol/kg)	TG	CHOL	HDL	GLU	GLY	FFA
Test Compound1	300	-48**	-8	+15	-31**	-14	NC
Fenofibrate (standard drug)	1000	-77**	-30**	+33**	-33**	-52**	-53**

** p value<0.001, values are mean + sd of 8 animals

These results show that the test compound 1 besides having sugar lowering activity, has the added advantage of antihyperlipedemic activity as well.